Message

From: Hopkins, Yvette [Hopkins.Yvette@epa.gov]
Sent: 7/24/2018 12:25:49 PM
To: Dawson, Jeffrey [Dawson.Jeff@epa.gov]
CC: Vogel, Dana [Vogel.Dana@epa.gov]; Teter, Royan [Teter.Royan@epa.gov]
Subject: RE: Request for input- Importance of the GLP Audit and Inspection Program-CLA assertions about GLP inhibiting registrations and other claims

Jeff,
Thanks for HED's comments, as they support other information gathered about this topic.
Ex. 5 Deliberative Process (DP)
Yvette

From: Dawson, Jeffrey
Sent: Tuesday, July 24, 2018 7:59 AM
To: Hopkins, Yvette <Hopkins.Yvette@epa.gov>
Cc: Hopkins, Yvette <Hopkins.Yvette@epa.gov>; Vogel, Dana <Vogel.Dana@epa.gov>
Subject: RE: Request for input- Importance of the GLP Audit and Inspection Program-CLA assertions about GLP inhibiting registrations and other claims

Yvette,

I am glad we talked about the GLP issues raised by Ray McAllister's note. The following bullets more or less summarize the routine HED experience related to GLPs as we discussed:

- GLPs provide a critical level of surety with the scientific data generated by the registrant stakeholder community and all of the CROs which are used by the industry (~1400 or so as noted in CLA submission). We rely on that surety to ensure that regulatory outcomes are based on rigorous scientific data. They also stand in stark contrast to the ongoing "raw data" issue which is currently ongoing related to the use of published data in regulatory actions.

- To the best of our knowledge we have never heard of a GLP issue impeding scientific analysis and risk assessment development unless it was an actual issue associated with the quality and reliability of data under consideration.

- We very rarely hear of GLP audits and compliance inspections. No major issues have been identified in recent history that we are aware of which would impact HED.

- HED is not routinely asked for prioritization of GLP audits it desires.

- With many newer technologies being implemented (e.g., broader use of in vitro testing methods as alternatives to animal testing) it is likely that new CROs will possibly be coming on line. With such events likely in the near future it is recommended that this phenomena be considered in a strategic planning approach to ensure these newer facilities and/or capabilities are adequately considered in the program.

Thanks and hope this helps,

Jeff

Jeffrey L Dawson
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Health Effects Division
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From: Hopkins, Yvette
Sent: Friday, July 20, 2018 1:17 PM
To: Echeverria, Marietta <Echeverria.Marietta@epa.gov>; Vogel, Dana <Vogel.Dana@epa.gov>; Goodis, Michael <Goodis.Michael@epa.gov>; McNally, Robert <Mcnally.Robert@epa.gov>; Pease, Anita <Pease.Anita@epa.gov>
Cc: Mosby, Jackie <Mosby.Jackie@epa.gov>; Wire, Cindy <Wire.Cindy@epa.gov>; Anderson, Brian <Anderson.Brian@epa.gov>; Dawson, Jeffrey <Dawson.Jeff@epa.gov>; Rosenblatt, Daniel <Rosenblatt.Dan@epa.gov>; Overbey, Dian <Overbey.Dian@epa.gov>; Weiss, Steven <Weiss.Steven@epa.gov>; Isbell, Diane <Isbell.Diane@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>; Keigwin, Richard <Keigwin.Richard@epa.gov>
Subject: FW: Request for input- Importance of the GLP Audit and Inspection Program-CLA assertions about GLP inhibiting registrations and other claims

All,
As you can read below, CLA has leveled complaints to OECA about GLP resources and deployment. OECA asked for an informal check in with the program on one particular assertion regarding GLPs hindering obtaining registrations, although senior management is interested in the issue more broadly.
I am not certain who to ask in your division about these issues, so if you would direct this to your relevant POC, FEAD will be happy to collect the information.
OECA would like the answer to the question about deleterious effects on registration by next week, but we have been given no time for the other GLP aspects.
Thanks for any assistance on this.

Yvette S. Hopkins
Enforcement Coordinator
Field and External Affairs Division, Office of Pesticide Programs
703 308-1090

The gods had condemned Sisyphus to ceaselessly rolling a rock to the top of a mountain, whence the stone would fall back of its own weight. They had thought with some reason that there is no more dreadful punishment than futile and hopeless labor. A. Camus

From: Messina, Edward
Sent: Friday, July 20, 2018 10:27 AM
To: Keigwin, Richard <Keigwin.Richard@epa.gov>; Mosby, Jackie <Mosby.Jackie@epa.gov>
Cc: Hopkins, Yvette <Hopkins.Yvette@epa.gov>; Wire, Cindy <Wire.Cindy@epa.gov>; Rice, Denise <Rice.Denise@epa.gov>
Subject: RE: Importance of the GLP Audit and Inspection Program- Q from OECA on GLP inhibiting registrations

Ex. 5 Deliberative Process (DP)

Ed

- The Good Laboratory Practice (GLP) program is a quality management system "intended to assure the quality and integrity of data submitted pursuant to sections 3, 4, 5, 8, 18, and 24(c) of FIFRA" (40 CFR Part 160.1, Scope and Applicability) and "to ensure the quality and integrity of data submitted pursuant to testing consent agreements and test rules issued under section 4 of the Toxic Substances Control Act (TSCA)" (40 CFR Part 792.1).
- In short, GLP assures the data submitted to the Agency, in support of registration applications, are of known and acceptable quality.
- The Agency does not perform its own studies but relies on the studies generated by industry. GLP inspections are the way in which the program ensures the integrity of these "outside" studies.
- The U.S. participates in OECD's Mutual Acceptance of Data (MAD) program, designed to garner international recognition of testing data in support of pesticide and chemical registrations. Currently, 31 member countries and 5 non-member countries participate in evaluating each other's testing programs.
- This means the U.S. will accept study data generated in these countries and evaluate them as if they were generated in the US, and *vice versa*.
- In addition to civil violations the GLP program has is the past uncovered criminal activity regarding the falsification of data.

Ed Messina
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From: Keigwin, Richard
Sent: Friday, July 20, 2018 6:29 AM
To: Mosby, Jackie <Mosby.Jackie@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Cc: Hopkins, Yvette <Hopkins.Yvette@epa.gov>; Wire, Cindy <Wire.Cindy@epa.gov>
Subject: RE: Importance of the GLP Audit and Inspection Program- Q from OECA on GLP inhibiting registrations

Ex. 5 Deliberative Process (DP)

From: Mosby, Jackie
Sent: Thursday, July 19, 2018 4:38 PM
To: Keigwin, Richard <Keigwin.Richard@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Cc: Hopkins, Yvette <Hopkins.Yvette@epa.gov>; Wire, Cindy <Wire.Cindy@epa.gov>
Subject: FW: Importance of the GLP Audit and Inspection Program- Q from OECA on GLP inhibiting registrations

Rick, Yvette was asked by OECA to weigh in on CLA's assertion, and she was going to reach out to the regulatory divisions. **Ex. 5 Deliberative Process (DP)**

Ex. 5 Deliberative Process (DP) Thanks, Jackie

Jacqueline E. Mosby, MPH
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From: Hopkins, Yvette
Sent: Thursday, July 19, 2018 4:22 PM
To: Mosby, Jackie <Mosby.Jackie@epa.gov>; Herndon, George <Herndon.George@epa.gov>
Cc: Wire, Cindy <Wire.Cindy@epa.gov>; Wormell, Lance <Wormell.Lance@epa.gov>
Subject: FW: Importance of the GLP Audit and Inspection Program- Q from OECA on GLP inhibiting registrations

Jackie,

Ex. 5 Deliberative Process (DP)

Yvette

From: Bodine, Susan
Sent: Thursday, July 19, 2018 12:07 PM
To: Kelley, Rosemarie <Kelley.Rosemarie@epa.gov>; Sullivan, Greg <Sullivan.Greg@epa.gov>
Cc: Starfield, Lawrence <Starfield.Lawrence@epa.gov>; Traylor, Patrick <traylor.patrick@epa.gov>
Subject: FW: Importance of the GLP Audit and Inspection Program

From: Ray McAllister [mailto:RMcAllister@croplifeamerica.org]
Sent: Thursday, July 19, 2018 9:49 AM
To: Bodine, Susan <bodine.susan@epa.gov>
Cc: Starfield, Lawrence <Starfield.Lawrence@epa.gov>; Morris, Jeff <Morris.Jeff@epa.gov>; Wise, Louise <Wise.Louise@epa.gov>; Beck, Nancy <Beck.Nancy@epa.gov>; Keigwin, Richard <Keigwin.Richard@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>; Letendre, Daisy <letendre.daisy@epa.gov>; Sharpe, Kristinn <Sharpe.Kristinn@epa.gov>; janet collins <jcollins@croplifeamerica.org>; Jay Vroom <JVroom@croplifeamerica.org>; Allison Jones (allisonjones@naicc.org) <allisonjones@naicc.org>
Subject: Importance of the GLP Audit and Inspection Program

Ms. Bodine:

On behalf of Crop Life America (CLA) and the National Association of Independent Crop Consultants (NAICC), we want to follow up the CLA visit with you on May 10 with more detail on the importance of the Good Laboratory Practice (GLP) Audit and Inspection program to the crop protection industry. We would welcome the opportunity to continue this conversation. I am taking the liberty of copying other EPA leaders with a stake in this program.

- We are concerned about a loss of vision within the management at the Environmental Protection Agency (EPA) regarding what the GLP program should do and be and accomplish.
- The GLP inspection and audit program is being starved of resources and personnel. In 1994, when the program was under the Office of Prevention, Pesticides, and Toxic Substances (OPPTS), there were 19 inspectors, 6 support staff, and a contractor supporting the GLP program. Currently in the Office of Enforcement and Compliance Assurance (OECA) there are 4 inspectors and no support staff.

- A reasonable frequency of audit and inspection of the individual labs and facilities is necessary to assure EPA of the quality and integrity of the data supporting pesticide product registrations, as required by law, regulation, and international agreement.
- There are some 1400 laboratories, facilities, and field sites in the US participating in GLP research on pesticides. With current staffing of the audit and inspection program, keeping up with that number of facilities seems like an impossible task.
- By comparison, the burden of other GLP audit and inspection programs is more balanced, for example: US-FDA (300 labs, 75 inspectors); Canada (40 labs, 23 inspectors); UK (100 labs, 8 inspectors); Germany (160 labs, 53 inspectors). Many of these inspectors in other programs are part time.
- If inspections are not conducted with sufficient frequency, registrants may feel obligated to take their research to foreign contract research organizations (CROs), leading to loss of business for US laboratories.
- The US is obligated as a member of the Organization for Economic Cooperation and Development (OECD) to comply with requirements of formal OECD Decisions regarding GLP and audits and inspections. This has a direct bearing on the ability of US industry to operate internationally. Among other things, these requirements cover:
    - The nature and frequency of audits and inspections;
    - Providing statements of such audits and inspections to foreign governments in a timely manner.
- Historically, US has had a preeminent role in the development and management of the GLP and Mutual Acceptance of Data (MAD) programs under OECD. In recent years, EPA participation in the OECD GLP Committee and other international forums has been curtailed, resulting in loss of leadership, where the US should be in the forefront. The US should maintain active engagement in moulding and shaping the future direction of MAD.
- Because the EPA does <u>not</u> issue compliance certificates to GLP facilities, the inspection closure letters from EPA are vital in the registration submission process to many other countries, to assure studies have been conducted in a GLP-compliant facility. Lack of the closure letter creates a significant barrier to acceptance of US studies by other countries.
- Registrants experience delays in registrations when they have to obtain a closure letter from the laboratory to send to the monitoring authority in the foreign government. The current practice is to obtain the closure letter in advance to include with the study report in the registration application, and not wait for the monitoring authority to make a request.
- New CROs have a hard time breaking into the business, because of lack of inspections and lack of the ability to be inspected.
- The industry – both registrants and CROs – have a great deal of confidence in and respect for Francis Liem who has led the audit and inspection effort for many years. The Agency must maintain this level of experience and expertise.
- Interaction of audit and inspection staff with industry has been curtailed. We depend on frequent interaction with them in meetings and conferences to keep up to date on the latest developments in GLP.
- The prospect of additional funding authorized by the Pesticide Registration Improvement Act (PRIA) to bolster the GLP program is heartening. It is the clear intent of PRIA legislation that this additional funding supplement, and not replace, current funding from appropriations. It is essential that the new funds set aside for this purpose be spent exclusively on the GLP program.
- In 2016 there was serious consideration of moving the audit and inspection program to the Office of Chemical Safety and Pollution Prevention (OCSPP). We felt then and still feel now that this would be a very positive step for the program.
    - The GLP program began in OPPTS {now known as OCSPP), and was located there until the mid 1990s.
    - The principle purpose of EPA's GLP program is to support the registration decisions made by the Office of Pesticide Programs (OPP) within OCSPP.
    - With such an organizational change, the GLP program could be more responsive to the audit and inspection needs of OPP for specific studies and facilities.
    - Administration of funds from product maintenance fees under PRIA for the GLP program would be simpler and more straightforward in OCSPP, which administers all other PRIA funds.
    - The GLP program does not audit or inspect research performed by OPP, so the organizational connection would not represent a conflict of interest.

    - OCSPP can maintain the appropriate organizational structure to assure independence of the GLP program.
- A robust GLP program in full compliance with the OECD MAD requirements demonstrates to all stakeholders the integrity of industry-supported and generated data that underpin pesticide registrations in the US and around the world. The EPA has a significant responsibility to vigorously defend its Pesticide Programs, and the GLP program should contribute in that regard.

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